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(21) International Application Number: PCT/US91/04863 (22) International Filing Date: 10 July 1991 (10.07.91) (30) Priority data: 550,827                      10 July 1990 (10.07.90)                      US (71) Applicant: BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM [US/US]; 201 West 7th Street, Austin, TX 78701 (US). (72) Inventors: NICOLSON, Garth, L. : 2611 Valley Manor, Kingwood, TX 77339 (US). IRIMURA, Tetsuro : 5205 Evergreen, Bellaire, TX 77401 (US). NAKAJIMA, Moto- wo : 5803 Dryad, Houston, TX 77055 (US). (74) Agent: HODGINS, Daniel, S.; Arnold, White & Durkee, P.O. Box 4435, Houston, TX 77210 (US).	(51) Designated States: AT, AT (European patent), AU, BE, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GE, GE (Eu- ropean patent), GN (OAPI patent), GR (European pa- tent), HU, IT (European patent), JP, KP, KR, LE, LU, LU (European patent), MC, MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European pa- tent), NO, PL, RO, SD, SE, SE (European patent), SN + (OAPI patent), SU, TD (OAPI patent), TG (OAPI pa- tent).  Published With international search report. Before the expiration of the time limits for amending the claims and to be republished in the event of the receipt of amendments.	
(54) Title: GLYCOSAMINOGLYCAN DERIVATIVES AND THEIR USE AS INHIBITORS OF TUMOR INVASIVENESS OR METASTATIC PROFUSION-II		
(57) Abstract  The present invention comprises a method for impeding the formation of tumor metastasis or tumor invasiveness in a host. Such inhibition comprises administration to the host of a glycosaminoglycan derivative substantially devoid of anticoagulation activity and is an effective inhibitory of heparanase activity. Such a glycosaminoglycan derivative may be provided by purchase or synthesis as directed herein. Parenteral administration to a tumor-bearing host of the glycosaminoglycan derivative results in the exposure of host-borne tumor cells thereto. Such exposure to effective levels of the derivative results in the inhibition of tumor heparanase activity and a lessening of invasiveness and metastatic spread. Heparin, a glycosaminoglycan particularly effective as a heparanase inhibitor and an anti-clotting agent, is a preferred glycosaminoglycan for derivatization. Upon derivatization according to the present invention heparin may be converted into a glycosaminoglycan derivative substantially devoid of anticoagulant activity but yet being an effective inhibitor of heparanase activity. Mere reduction of heparin carboxyl groups results in the production of a glycosaminoglycan derivative inhibitory to heparanase activity but without substantially anticoagulant activity. non-anticoagulating, heparanase-inhibiting glycosaminoglycan derivatives may also be prepared from heparin, for example, by: at least partial N-desulfation and then N-acetylation; or N-, O-desulfation followed by N-resulfation.		

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